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Evaluation of *oprD* Gene Expression in Carbapenem-Resistant *Pseudomonas aeruginosa* Strains Isolated From Severe Burn Patients With Secondary Infection

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Background: *Pseudomonas aeruginosa* is the most common pathogen isolated from severe burn patients with secondary infection. Since high resistance to most types of antibiotics is common among these bacteria, the treatment of infections caused by these agents is very difficult. Loss of oprD proteins from the outer membrane of bacterial cells causes a significant decrease in the sensitivity of *Pseudomonas aeruginosa* to carbapenems.

Objectives: This study was performed to investigate the prevalence of carbapenem-resistant strains of *Pseudomonas aeruginosa* in burn patients with secondary infection and also to evaluate *oprD* gene expression as a possible resistance mechanism to carbapenem in isolated carbapenem resistant *P. aeruginosa* strains.

Patients and Methods: One-hundred and eighty-nine clinical isolates of carbapenem resistant *Pseudomonas aeruginosa*, isolated from burn patients, were identified by microbiological methods followed by determination of antibiotic resistance pattern by the Kirby-Bauer procedure. The expression of *oprD* gene was determined by quantitative real-time polymerase chain reaction (PCR).

Results: Our study showed that 94.2% of the isolates were resistant to imipenem, 99.5% to meropenem, and all were resistant to ertapenem. The *OprD* gene expression among carbapenem resistant *Pseudomonas aeruginosa* isolates showed a 2×10^{-3} to 0.5 times decrease compared to the standard sensitive strain ($P < 0.05$).

Conclusions: The results of this study indicated that a decrease in *oprD* gene expression is an important mechanism of resistance in carbapenem resistant *Pseudomonas aeruginosa* isolated from severe burn patients with secondary infection.

Keywords: Drug Resistance; *OprD*; *Pseudomonas aeruginosa*

1. Background

Pseudomonas aeruginosa are gram negative bacteria distributed in soil, water, skin flora, and the majority of man-made environmental sources, worldwide (1). Regarding the presence of widespread antibiotic resistance among the clinical isolates of *P. aeruginosa*, this organism is considered as one of the most important bacterial agents associated with nosocomial infections, for which the process of successful treatment is frequently hard to achieve (2, 3). These bacteria are known as the second most common bacterial agents in burn infections (4, 5) and are also ranked third, after *Staphylococcus aureus* and *Escherichia coli,* amongst the most frequent agents of nosocomial infections (6). *Pseudomonas aeruginosa* is amongst common causes of mechanical ventilation-associated pneumonia, surgical site infection, hospital-acquired urinary tract infection and bacteremia in patients admitted to intensive care units (ICUs) (7, 8). This organism is reported to be the most prevalent pathogen isolated from patients with secondary infection following severe burn injury (9). Currently, the prevalence of hospital Multi-Drug Resistance (MDR) strains of *P. aeruginosa* is increasingly on the rise because of widespread clinical application of antibiotics throughout the world (10), making the treatment of infections caused by these MDR organisms very complicated (2, 3).

Carbapenems such as imipenem and meropenem are amongst the most important antibacterial agents routinely used in treating infections caused by MDR *Pseudomonas aeruginosa* strains (11-13). Generally, controlling the prevalence of these MDR organisms is difficult as *P. aeruginosa* has intrinsic antibiotic resistance against different antibacterial agents (10). There are several mechanisms through which resistance against diverse antibacterial agents occurs by this organism (14). Resistance to different antibacterial drugs generally occurs either as the result of the combination of different mechanisms in a